THE THERAPEUTIC USES OF WINE

(A Summary)

This summary of THE THERAPEUTIC USES OF WINE is published by the Wine Advisory Board, an agricultural industry administrative agency established and operating pursuant to the marketing order for wine, issued and made effective under the authority of the California Marketing Act of 1937.

WINE ADVISORY BOARD, SAN FRANCISCO, CALIFORNIA

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FOREWORD

The history of wine in medical practice is one of marked change in the various ages of Man.

Since Hippocrates first advocated the use of wine in medical practice, recommendations have come from great men down through the ages, and the medical uses of wine have fluctuated from the universal almost to the disappearing point and back again.

An entire generation of physicians lost touch with the medical lore of wine in the United States following the first World War. Meanwhile, the rapid development of experimental medicine took place, and the values of hundreds of newer therapeutic substances were quickly measured and made known, while wine was left to rest on what the older generation had empirically determined.

Actually, few other substances available to Man have been as widely recommended for their curative powers, as has wine. From Aesculapius to modern times, it has had a most imposing procession of advocates. Pliny, Athenaeus, Horace, and Columella chronicled the virtues of wine in ancient times. Paul, in the Bible, advises Timothy, ‘‘Drink no longer water, but use a little wine for thy stomach’s sake and thine often infirmities,’’ and Pasteur has written, ‘‘Wine is the most healthful and the most hygienic of beverages.’’

In comparatively recent years, there has developed a demand within the medical profession that the true values or deficiencies of wine be ascertained; that fact be separated from folklore by the application of impartial analysis and the study of those factors which are scientifically measurable. Accordingly, in 1939, there was initiated under the guidance of the Society of

Medical Friends of Wine, a research program of the medical and chemical values and uses of wine. Several qualified research institutions have participated in the program and individual projects have been supported by the Wine Advisory Board, an agricultural industry administrative agency established under authority of the California Marketing Act of 1937, and interested in wine growing and marketing as an important agricultural industry in the State of California.

Much of the credit for the collection of the facts included and evaluated in this summary is due to the research project in the bibliography of the medical and chemical uses of wine being compiled in the University of California Medical School.

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THE THERAPEUTIC USES OF WINE

WINE AS A FOOD

Food is defined by the dietitian [27] as a substance which when taken into the body yields heat and energy, supplies the elements for growth and replacement of worn-out tissue, or serves as a metabolic regulator of protoplasmic activity.

The term food, according to legal decree,[113] includes "everything that is eaten or drunk for nourishment of the body. Any substance that is taken into the body which serves true organic action to build up the normal tissues or to supply the waste tissue is a food."

The use of wine as a food dates back to the beginning of history. In the ancient history of Egypt [34, 117] and Greece,[65] references are found in which men used wine as a food. There are records that seem to indicate that even the stone-age man was not without his wine.

The Egyptians were extensive vineyardists and wine was in their diet.[34] Four general grades of wine were known by the classes that were able to afford the quality of each, the least expensive wine being known as the "fishermen's wine," which seems suggestive of its probable quality.

The place of wine on the table is frequently alluded to in Biblical history.[118]

Wine contains both nutritive and nonnutritive [27] food elements. The nutritive or energy element is derived from the carbohydrate and protein content of the grape. The nonnutritive or maintenance elements, the minerals and vitamins, likewise derived naturally from the grape, are present in the proportions required in a complete food. Thus, wine is an easily obtainable pleasant food, the caloric content of which is balanced by its natural mineral and vitamin content.

The simple sugars are recognized as the most readily available and most easily assimilated source of caloric energy. In the human all compound sugars are broken into single sugars, stored as glycogen, and utilized by the tissues for energy production.

Present-day wines, depending upon type, usually contain from $\frac{1}{4}$ to 10 per cent of simple sugars. These simple sugars are principally dextrose or glucose and levulose or fructose.[5] Levulose, with a relative sweetness of 173, has its excessive sweetness balanced by dextrose with its relative sweetness of 74.[21]

Parisi, Sacchetti and Bruini [149] found that wine-musts, prior to fermentation, have a levulose-dextrose ratio of greater than one, but that during fermentation the levulose fermented more rapidly than the dextrose and as a result the predominant sugar in the finished wines was dextrose. The determination of the dextrose-levulose ratio has been used by wine growers and analytical laboratories as a means of determining the completeness of fermentation.[4]

Alwood [3] found no sucrose in the grape or wine of the true *Vitis vinifera*, although certain native species had small amounts present. When sucrose is found in a wine it is generally considered to be present only as an adulterant.[4]

Physiologically, the uses and benefits derived from the administration of dextrose are known to every physician. Its quick absorption and complete availability are of protective value to all the organs of the body. Connor [50] and Chaikoff [43] have pronounced dextrose to be the single most important factor in the prevention of fatty livers, which condition they believe to be the precursor of the cirrhotic liver.

It has been established that alcohol does not impede the rate of absorption of dextrose. Scanzoni,[165] Tappeiner,[180] Brandl,[26] Higgins,[85] and Edkins and Murray,[60, 61, 62] all have published experimental evidence demonstrating this fact.

Atwater and Benedict,[9] and Neumann,[137] demonstrated that 95 per cent of the caloric energy of alcohol is available for use. Recently, Richter [157] has shown that rats will maintain normal weight and health when as high as 40 per cent of the caloric intake is in the form of alcohol. The alcohol in wine (normally 10 to 13% in table wines and 19 to 20% in dessert wines) is therefore useful as a source of caloric energy.

It has been pointed out by Jolliffe [96] that increase in vitamin-free calories in the diet increases the need for thiamin. Wine is the only common alcoholic beverage containing proven quantities of the B vitamins. French investigators, principally Randoin [154, 155] have indicated, and Morgan [128] has published careful assays of the B content of wines and has found sufficient quantities of the vitamin complex to materially augment the daily vitamin intake.

Wine contains other organic material with food value, such as purines, inulins, pectins, fats, tannin, and glycerin. Though the amounts of these substances are small, each has its recognized value in modern therapy. There are other substances in wine, such as the aromatic organic esters, which defy exact chemical analysis but contribute to its pleasant aroma and bouquet.

The inorganic or mineral constituents of wine vary with the conditions under which the grapes have been permitted to mature. While the total content of such constituents is not large, present-day wines contain all of the 13 mineral elements which Underwood [185] has pointed out as necessary to maintain animal and human life. Amerine and Joslyn [5] list the mineral constituents of wine-musts, and comparisons made from their figures indicate that wine-musts have a favorable utilizable content of the seven most essential mineral elements, i.e., sodium, potassium, calcium, magnesium, chloride, phosphorus and iron.

Saywell [163] has made extensive studies of the iron in wine and finds that four-fifths of the iron present in wine is in the reduced ferrous form and is stable as such after long periods of aging. Tompsett,[183] in studying human and animal absorption of iron, finds that only reduced iron is absorbed from the intestine. The factors aiding this absorption are, first, a proper diet in the chemical sense, and, second, an adequate production of acid by the stomach. The iron in wine is in a proper chemical form and remains utilizable as such even after long periods of aging. Wine invokes a secretory response from the hypochlorhydric stomach as well as the normal organ. This is further discussed in following sections.

In the ordinary iron deficient diet of the average American, there is a place for wine as a source of easily available and readily assimilable iron. Fishbein, Calvin, and Heumann [71] demonstrated in children a significant hemoglobin rise after the daily ingestion of grape juice. Work now in progress indicates that the ingestion of wine increases the absorption of ferrous sulphate medication.[147] The use of moderate amounts of wine at mealtimes will supply the adult with an adequate daily iron supplement.[163, 190]

The potassium, phosphate and copper contents regularly noted by wine chemists are of individual importance in maintaining the normal heart action,[176] in dextrose metabolism,[63] and hemoglobin regeneration.[64, 188] Aluminum, manganese and other mineral elements are also present in trace quantities.

In summary, it may therefore be said that:

(a) Present-day wines contain considerable quantities, dependent on type, of natural dextrose derived from the grape, and not present as an adulterant;
(b) The dextrose in wine is absorbed readily and is easily assimilable, and is therefore highly desirable in the human diet;
(c) The alcohol in wine is readily available as a source of caloric energy;
(d) Wine contains proven quantities of the Vitamin B complex;
(e) The iron in wine remains stable after aging and is in the useful reduced ferrous form; and
(f) Wine contains, in addition, all the mineral elements essential to health.

ACTION OF WINE UPON THE DIGESTIVE ORGANS AND ITS USE IN DISEASES OF THE GASTRO-INTESTINAL SYSTEM

Beaumont[15] and Bernard[19] were the first to study scientifically the effects of alcohol ingestion. A great deal has been written since their time, but only recently has there been any consensus of opinion on the mechanism of the digestion of alcohol, which is a most complex problem because of the roles played by the central nervous system and the psychic conditioning reflexes.

All of the digestive organs are responsive to alcohol, and its effect on each organ varies with the concentration, amount and frequency of the quantity ingested.

Effects on the Salivary Glands

In human subjects Winsor and Strongin[201] noted an augmentation of the salivary flow for a ten minute period after the ingestion of moderate amounts of wine. The rate of secretion returned to a basal level after a period of one and one-half hours. The cause of the increase in salivary flow is not completely known. Chittenden[44] noted that the application of strong concentrations of alcohol to the tongue and buccal mucosa excited a flow of saliva, but that the introduction of alcohol directly into the stomach did not.

Ptyalin, the salivary starch digestive enzyme, is unaffected by the concentration of alcohol present in table wines.[45] The best opinion at present, Beazell and Ivy,[16] is that the origin of the increased flow is probably a direct sensitization of the secretory nerve endings in the gland itself. The concentration of alcohol in the saliva parallels the arterial blood alcohol level and the mechanism is probably that of direct diffusion. Linde,[114] Abels,[1] Vollenbruck,[189] Friedemann,[74] and others have made such extensive studies of this relationship that the salivary excretion levels are accepted in medico-legal work.

Effects on Tongue and Oral Mucosa

The direct irritative effect on the mouth from strong concentrations of alcohol present in spirituous liquor is common knowledge. However, the glossitis and stomatitis of the heavy drinker are caused not by the alcohol, but by the deficiency diseases induced by an inadequate diet. Blankenhorn and Spies [23] have found that these mouth lesions respond readily to concentrated vitamin therapy, even when the alcohol is not removed from the diet.

Effects on Esophagus

Because of the speed of esophageal passage and the unfitness of the mucosa for absorption, there is no esophageal absorption unless the esophagus has been previously damaged by the passage of or lavage with concentrated solutions of alcohol. (Webb, Mullenix, and Dragstedt.)[191]

Effects on Stomach

Ogden,[144] in an as yet unpublished work, has shown that table wines, and to a less extent dessert wines, increase the flow of gastric secretion. After ingestion of moderate amounts, 120 to 180 cc., of white table wine, he found the volume of gastric juice to be appreciably increased in the stomachs of normal human subjects.

That alcohol in concentrations of 7 to 20 per cent will augment the gastric flow has been shown by many physiologists, Bernard,[19] Saito,[161] Babkin,[10] Dragstedt,[58] Barlow,[12] and others, and this secretogogue effect has been used clinically in the Ewald test meal for many years.

However, the secretory augmentation after ingestion of wine differs from that of plain alcohol solutions in that the natural fruit salts, tartrates, phosphates and other constituents act as buffer salts, preventing any inordinate rise in acid strengths, and tend to prevent the rapid peak characteristic of unbuffered solutions. This buffering effect causes a tempered increase in flow which extends over a longer period and is more in harmony with the natural digestive and propulsive factors of gastric digestion.

Barlow [12] has studied the effect of varying concentrations of alcohol on the stomach and finds that concentrations above 20 per cent show definite evidence of irritation of the gastric mucosa. This irritation is accompanied by the outpouring of mucus, which is secreted by the glands of the stomach in an effort to protect themselves from the effects of the toxic concentration.

The increase in flow of pepsin after stimulation by alcohol has been noted by Kast,[98] Lönnquist,[116] Babkin,[10] and, recently, Krueger, MacIntosh [103] and others. The increase in pepsin is not of the same order as the increase in acid flow but because of the augmentation of total flow there is a definite quantitative increase in total pepsin produced. Haneborg [81] has shown that the ingestion of diluted alcohol with mixed meals caused an increase in the proteolytic power of the juice one and one-half hours after the ingestion of the meal. This is of importance to those persons suffering from inadequate gastric digestion of the usual mixed meal.

Stimulation of the flow of gastric juice by wine is definite although the mechanics of this stimulation are not yet completely determined. The psychic element from the ingestion of a pleasantly flavored beverage with a good bouquet is undoubtedly more important in the atmosphere of a well appointed dining room than in the laboratory where the fasting human subject must take his wine with a stomach tube kept in place for several hours.

Soresi,[170] who has administered wine by rectum, finds it well absorbed without irritation of the rectal mucosa. The general effects were not modified by unpleasant side reactions and an increase in appetite was noted.

According to Newman and Mehrtens,[142] Petrovich and Bokanowa,[150] Ivy and McIlvain,[92] alcohol is found to be as effective in increasing the flow of gastric juice when administered intravenously as when administered orally.

It may be assumed, therefore, that wine increases the gastric secretion (a) by direct nonirritative contact with the gastric mucosa, (b) by direct action on the secreting cells through diffusion from the blood stream, (c) by reflex stimulation through the vagus nerve, the sensory pathway being through the afferent nerves of the mouth, pharynx, or stomach, and (d) by lessening worry and mental tension and thereby releasing cerebral inhibitions.

Kast [99] in reviewing the previous literature comes to the conclusion that dilute concentrations of alcohol increase motility of the stomach while strong concentrations have a definite delaying action. This is borne out by the work of Carlson,[39] who found that after ingestion of concentrated alcohol the hunger contractions of the stomach were abolished from 24 to 48 hours.

Scott and Luckhardt,[167] in determining the effect of dosage comparable to the pre-dinner appetizer, gave two wine glassfuls of 20 per cent alcohol (the concentration of the usual dessert or appetizer wine) at five minute intervals and found definite hunger sensation present five minutes after ingestion. The increased hunger was accompanied by a relaxation of the gastric tension which persisted for somewhat less than an hour. With the present-day stress of living such a pre-dinner relaxation of the stomach should be an important factor in the prevention of the all too prevalent gastric disturbances.

In summary, therefore, it may be said that (a) wine is completely nonirritative to the mucosa of the stomach, (b) it causes definite increase in the flow of gastric secretions, (c) the increase of secretion is tempered by the action of the buffer salts present in the wine, (d) the ingestion of wine permits the stomach to relax, and (e) while alcoholic beverages are usually interdicted in cases of gastric complaint, wine, for the foregoing reasons, is not necessarily contraindicated.

Effects on Small Intestine

Because of the difficulties of the experimental approach to the digestion in the small intestine, few references are available in the literature. Empiric observation by many clinicians has found wine to be of value as an antispasmodic, and, therefore, of value in cases of intestinal colic. This empiric data is substantiated by Kyno,[105] who found that dilute concentrations of alcohol lessened the activity of the smooth muscle of the intestine.

Effects on Large Intestine

Little has been published on the effects of wine on the large intestine. It was an established fact for 600 years that seamen afflicted with diarrhea would hasten to ports where they could purchase young Barbera wine, which with its high tannin content would soon check the ailment. In the absence of Barbera, other young wines fermented on the tannin-containing skins often proved efficacious. Weissenbach[194] in the French literature has recommended the use of wine for treatment of mucous colitis, diarrhea and spastic constipation.

Adler, Beazell, Atkinson and Ivy[2] have recently found that alcohol in 20 per cent concentration increased the propulsive activity of the colon when determined in patients with colostomies. The same concentration when given to normal subjects was found to facilitate the gastro-colic reflex and thereby aid natural colonic evacuation.

Effects on Pancreas

Kuwschinski,[104] in 1886, was the first to demonstrate an increased flow of pancreatic juice after the administration of alcohol. This has been borne out by all physiological reports published since. Gizelt [78] after ligating the pylorus found alcohol to be an effective pancreatic stimulant when administered either by stomach or by rectum. Fleig [73] demonstrated the effect to be valid when the alcohol was introduced into a closed intestinal loop. This increase of flow is accompanied by a proportionate increase in the output of the pancreatic enzymes, which are regarded by most physiologists as a most important single digestive factor.

The concentration of alcohol in the intestine is always quite dilute because of the chylous mixture present in the lumen. This concentration is sufficiently low so that the enzyme activity is not hampered. Buĭkov and Fursikov [32] found steapsin to have increased fat digestive activity when acting in the presence of alcohol.

Because of the increased rate and amount of pancreatic secretion after ingestion of wine, it is felt, by Myers and Keefer,[134] Émile and André,[66] and Clark,[47] that wine is contraindicated in cases of acute inflammation of the pancreas and perhaps in conditions with associated biliary dysfunction.

Effects on Liver

Studies of the effect of alcohol on the flow of biliary secretions have dealt mainly with the effects of single intoxicating doses. In each case the flow has been found to be decreased. With the administration of 15 to 20 cc. doses in mild concentrations, Salant [162] noted a definite augmentation of the biliary flow.

Okada [145] verifies these observations by demonstrating that 200 cc. of a 10 per cent solution of alcohol caused a 20 to 25 per cent increase in the hourly flow from biliary fistulae. This increased biliary flow, in conjunction with increased and enhanced pancreatic fat enzyme function, may make the wine drinker better able to digest fatty meals.

As mentioned in a previous section, wines of high dextrose content should have an anticirrhotic property because of the role of dextrose in preventing fatty degeneration of the liver.

It is of interest in accordance with the above to note that Leary [107] finds the incidence of gall bladder stones among subjects who had been users of alcohol to be only one-seventh of the incidence in diabetics and about one-third of the incidence expected of a random sample.

ACTION OF WINE ON THE KIDNEYS AND URINARY PASSAGES AND ITS USES IN DISEASES OF THE KIDNEYS

The effect of alcohol on the kidneys has been under discussion for many years. In 1827, Bright [28] considered the abuse of alcoholic beverages a factor in the causation of nephritis. Early in 1846, Dickinson [72] reported that he was unable to find any greater incidence of renal disease in patients who died of delirium tremens than in those who died from accidental causes. Fishberg,[72] in his modern monograph on nephritis and hypertension, is in complete accordance with Dickinson's refutation.

Wegelin,[193] Ziegler and Horner,[204] Cohnheim and Marchand [49] have presented pathological evidence showing that the kidney vasculature in users of alcohol is unimpaired. In repeated experimental administration of moderate concentrations of alcohol, Friedenwald [75] and MacNider [118] found no evidence of pathological changes in the kidneys. This has been verified by Bruger, Localio and Guthrie.[30, 31] Fahr [69] states that alcohol has no deleterious effect on the kidney.

The kidneys excrete very little of the alcohol absorbed by the intestinal tract.[138] The concentration of alcohol in the urine is markedly similar to that in the blood, a fact [14, 197] recognized in medico-legal work. Miles [126] in studies of ingestion of single large doses of alcohol found that only 1.2 per cent to 1.6 per cent was excreted in the first two hours, after which the rate fell off markedly. With slower absorption rates, this excretion was even less. Haggard and Greenberg [80] found that only 2.4 per cent to 4.3 per cent of the alcohol ingested was excreted as such by the kidney in 16 hours. It would appear from the foregoing that there can be little irritative effect on the ureters and bladder from the moderate use of staple temperate beverages.

In the treatment of nephritis, authorities such as Mosenthal,[129] Van Noorden,[186] and Fishberg [72] find that alcohol is not contraindicated and, in fact, prescribe it in moderate amounts to enhance appetite and increase the receptiveness of the patient to the prescribed diet.

The diuretic effect of low concentrations of alcohol has been noted by many workers throughout the years. In 1886, Simanowsky [169] showed that ingestion of a liter of wine produced a greater output than a like amount of water. This fundamental observation has been confirmed by Miles,[126] Januskiewicz,[94] Carpenter,[40] Mosonyi and Gömöri,[130] Murray,[133] Raso,[156] Iida [91] and DiMacco.[54]

Quite recently, Bruger, Localio and Guthrie,[30,31] noted that this diuretic response was greater in those patients afflicted with acute and chronic diffuse glomerular nephritis. A similar observation was made by John,[95] who found a greater diuretic response in patients with renal insufficiency due to hypertension than in normal subjects.

The cause of this diuresis has been discussed by Bastedo,[13] who ascribes it to a secondary dilatation of the renal arterioles permitting a greater flow of blood to the glomeruli with resultant increased output due to the increased availability of oxygen to the glomerular cells. The increased intake of fluid, he concludes, is an important additional factor.

Mrak and Fessler [131] bring out that the natural fruit salts and simple sugars present in wine make it of special value in promoting diuresis. They find the presence of buffer salts as found in wine prevents the acidosis which ordinarily follows the ingestion of alcohol. The composition of the wine is not changed from the normal, despite the diuresis.

Natural tartrates and phosphates present in the grape constitute a source of alkaline reserve. Clause [48] in a study of urinary effects of ingestion of grape products noted an increased output of organic acid, primarily uric and citric acid, and a greater alkalinizing effect on the urine. This is borne out by Saywell,[164] who administered large quantities of grape products to students on a basal diet and found the ammonia output lessened and the urine more alkaline with an increase in the alkaline ash.

In summary, it may be said that wine is beneficial to the kidneys because:

(a) It increases the blood flow to the glomeruli;
(b) It spares the alkaline reserve of the body;
(c) It promotes a mildly alkaline urine;
(d) It increases the flow of urine, and
(e) It is nonirritative to the kidneys, ureters, and bladder.

ACTION OF WINE ON THE CARDIO-VASCULAR SYSTEM

The eminent English physician Heberden,[84] in 1772, was the first to publicly recognize the beneficial effects of small amounts of brandy given orally for the relief of the pain of angina pectoris. In modern times, eminent cardiologists such as P. D. White,[196] recommend the use of brandy for the relief of anginal pain. Clark[46] believed this relief was due entirely to stimulation of sensory nerves. More recently, Stockton[177] and also Bishop[22] find that vasodilatation of the coronary arteries is the cause of the relief of pain.

This same vasodilating effect on the peripheral blood vessels is responsible for the feeling of warmth following the use of alcohol. This phenomenon has been studied and verified by many workers, among them Dixon,[56] Hare,[82] Hunt[88] and Starling.[175]

Cook and Brown,[52] of the Mayo Clinic, made a careful study of skin temperature following the administration of 0.5 cc. of alcohol per kilogram of body weight in a large group of patients afflicted with thrombo-angiitis obliterans, Raynauds disease, and arteriosclerosis with thrombosis. They found alcohol to be a more effective dilator than acetyl choline, and very effective in relief of the pain frequently present in severe forms of obliterative vascular disease. The increased circulation was marked by a rise in skin temperature, relief of pain, and healing of visible ulcerous lesions.

In studies on the isolated mammalian heart, Loeb[112] found that perfused alcohol in strengths of 0.13 to 0.3 per cent had a stimulating effect, increasing the stroke output. This work was confirmed by Bachem[11] and Dixon,[56] in a more elaborate heart-lung preparation. These workers found that when alcohol was added to the perfusing solution a definite improvement in the action of the heart occurred.

Sulzer and Cannan[179] noted that concentrations of 0.1 to 0.2 per cent of alcohol in the perfusing fluid caused coronary dilation and increased the output, but that in a concentration of 1.0 per cent the heart action was decidedly impaired. This concentration is well beyond physiological limits. Newman[139] points out that blood concentrations above 0.5 per cent are usually incompatible with human life.

Kootataladse,[102] in work as yet unconfirmed, isolated a substance from wine that in dilutions of 1 :500,000, increased the coronary flow, and doubled the output of the isolated mammalian heart. This effect was independent of the alcohol. The substance, an amine, was soluble in alcohol and water and was found only in fermented grape juice.

Many clinicians have noted that the incidence of coronary thrombosis is less among users of alcoholic beverages. The well founded clinical impression that there is a lessened incidence of coronary occlusion among regular consumers of beverage alcohol has been significantly stated and confirmed by Cabot,[35] Master, Dack and Jaffe,[122] and Leary.[108] Fahr [68] and Wells [195] found no increase in the incidence of this disease in similar groups of human subjects. Ruffer [160] in a significant study among Mohammedans (known abstainers) found that the incidence of sclerosis of the coronary arteries was greater than would be expected in a random sample.

Leary [107] observed that the incidence of arteriosclerosis among those who consumed alcohol was one-half that of a normal random population and only one-sixth that of diabetics. He attributes this phenomenon to the increased solubility of cholesterol in dilute solutions of alcohol. Eberhard [59] has experimentally confirmed the findings of Leary by feeding rabbits a diet high in cholesterol to which alcohol was added. Wilder [198] noted that diabetics (who suffer from disturbed cholesterol metabolism) who received alcohol therapeutically did not develop arteriosclerosis as readily as those who did not receive alcohol.

The use of moderate amounts of alcohol has little effect on the blood pressure. Lieb [111] and Cabot [35] noted no effect whatsoever on the blood pressure readings of hospitalized patients to whom alcohol was administered. On the other hand, intemperate consumption and toxic dosages of alcoholic beverages frequently result in a depression of the blood pressure. McDowall [123] states that "in therapeutic doses alcohol reduces venous pressure in man. . . ."

In conclusion, it may be stated that wine and brandy may be of therapeutic value in:

(a) Relieving the pain of angina pectoris;

(b) Relieving the pain and improving the circulation of the extremities in obliterative vascular diseases;

(c) Increasing the output of the heart;

(d) Decreasing the incidence of arteriosclerosis and coronary sclerosis, and

(e) Reducing the venous pressure.

ACTION OF WINE ON THE RESPIRATORY SYSTEM

The physiological effects of beverage alcohol upon the lungs are minimal. It may be both absorbed and excreted by the lungs. Carpenter [41] in metabolic studies found that alcohol was absorbed from the inspired air during exercise. He noted no adverse effect on the lung tissue from the inhalation.

Le Breton [109] noted that the alcohol level of blood in the alveolar capillaries is rapidly equilibrized with that of the systemic circulation. Any volatile substance in the alveolar blood should and does readily diffuse into the alveolar air in accordance with Henry's law of diffusion of gases. Harger, Lamb and Hulpieu,[83] and Southgate and Carter [173] agree that 2 liters of expired air contain as much alcohol as 1 cc. of blood. In true alveolar air Haggard and Greenberg [80] found the ratio to be 1142:1, and estimated that as much as 7 per cent of the alcohol oxidized might be excreted via the pulmonary ventilation.

Hunter and Mudd, [89] Robinson and Selesnick [159] and McFarland and Barach [124] have investigated the effect of forced increase of ventilation on the rate of alcohol excretion. They noted a definite clinical improvement during the inhalation of stimulating mixtures of oxygen and carbon dioxide. Newman and Card [141] found after careful study that the rate of excretion, although increased during inhalation of the gas, rapidly returned to its former rate on withdrawal.

The rate of respiration is increased momentarily following the oral ingestion of concentrated alcoholic beverages due to stimulation of the sensory reflexes of the mouth and pharynx. Wines when taken by mouth cause little if any sensory shock and therefore this momentarily increased ventilation does not take place.

Brooks [29] found that solutions containing 50 to 60 per cent of alcohol caused no increase in rate, rhythm or depth of ventilation when administered either by stomach tube, gastric fistula, or intravenously. This was corroborated by Hyatt.[90] In basal metabolic studies, Grubbs and Hitchcock [79] found that there was no significant change in the ventilation equivalent or in the alveolar carbon dioxide content following the ingestion of 10 per cent alcohol. Furthermore, they found no evidence of any specific dynamic effect of alcohol on the basal metabolic rate.

At the turn of the century it was customary to use alcohol in the treatment of acute respiratory diseases. However, Capps and Coleman,[38] Weeks [192] and others demonstrated that those patients receiving alcohol in quantities during the acute phase of pneumonia had a higher mortality than the control group. These studies led to the discontinuance of the use of alcohol in acute pneumonia.

Conversely, the mortality in pneumonia is high in the habitually alcoholic patient. In consideration of this difference in mortality Langmead and Hunt [106] call attention to the fact that the immoderate drinker found in the large public or charity institution has in addition often violated fundamental hygienic rules.

Although wine is probably contraindicated in the acute phase of pneumonia, Willcox [200] and Cornwall [53] have recently pointed out the value of judicious administration of wines and light beverage alcohol during the convalescent period. They consider the improvement in appetite and promotion of the general feeling of well-being derived from the use of wine to be of definite value.

Cecil,[42] in stressing the importance of adequate daily fluid intake of the patient with influenza, recommends the use of wine together with a light diet.

In summary it might be said:

(a) Wine in moderate dosages has little effect upon the normal pulmonary physiology;

(b) Wine is contraindicated in the acute phases of pneumonia, and

(c) Wine is of definite value in the period of convalescence from respiratory as well as other diseases.

ACTION OF WINE ON THE NERVOUS SYSTEM AND THE MUSCLES

Lee and Salant [110] were among the first to study the effect of alcohol on voluntary muscle. They found that isolated frog muscle when perfused with 10 per cent alcohol was able to perform more work before exhaustion set in. Scheffer [166] verified these experiments. Lombard [115] found that in human subjects small quantities of Claret wine increased the amount of muscular work for a period of about one hour after its ingestion. Each observer noted that muscular contractions were performed with greater ease and rapidity. Many observers, notably Rivers,[158] have noted that large doses of alcohol depress muscular function. Canzanelli, Guild and Rapport,[37] Carpenter,[41] and Nyman and Palmlov [143] found that the increased muscular exertion did not increase the rate of combustion of the ingested alcohol.

Masserman and Jacobson,[121] studying the sedative action of alcohol on the central nervous system, determined that dilute concentrations of alcohol (as found in the blood of those who have partaken moderately of dilute beverages) increased the electrical excitability of the hypothalamus with resultant stimulation. Larger doses caused depression of the hypothalamus. Newman [138] is in sympathy with this view. Gantt [76] found that the unconditioned reflexes are less affected by depressing dosages of alcohol than are the conditioned reflexes.

Mullin, Kleitman and Cooperman [132] attached a recording device to the bed of sleeping human subjects who had previously ingested a wine glass full of alcohol in concentration equivalent to that in Port wine and found the tossing movements of light sleepers definitely decreased during the first half of the night.

At present clinicians and experimenters, Minot, Strauss and Cobb,[127] Spies [174] and Strauss,[178] believe that neuritides, pellagra, certain encephalopathies and Wernickes disease are due directly to vitamin deficiency and only indirectly to alcohol. Askey [7] points out that a diet exclusively of alcoholic beverages will cause deficiency disease in much the same manner as a diet composed exclusively of any single dietary item. Campbell and

Biggart[36] believe that this mechanism of dietary deficiency is undoubtedly responsible for many of the so-called alcoholic psychoses.

Newman[140] found that the administration of 10 per cent alcohol to a group of schizophrenics and psychoneurotics increased their rapport, and suggested the use of alcohol in helping to establish these diagnoses. Kantarovich and Constantinovich[100] noted improvement in four cases of catatonia after the administration of brandy as a therapeutic measure. Trapp and Schube[184] found that the administration of dilute solutions of alcohol were of value in the diagnosis and treatment of a group of schizophrenics, manic-depressives, and mental deficients.

In the treatment of severe Parkinsonism, Fabing and Zeligs[67] reported that the satisfactory results derived from the use of a wine extract of Bulgarian belladonna root have not been achieved when the wine was supplanted by U.S.P. alcohol in the extraction. Neal and Dillenberg[135] and many others have made the same observation, and all agree that the most satisfactory results are achieved with the use of white table wine.

Although it is well established that beverage alcohol does not contribute to the accuracy of muscular coordination, there are specific instances in which its use may be of value in the diagnosis and treatment of disorders of the nervous system and the muscles.

THE USE OF WINE IN DIABETES MELLITUS

Wine has occupied a prominent and valuable position in the diet of the diabetic under both present-day and pre-insulin methods of treatment. Prior to the advent of insulin, energy foods that could be utilized without exaggerating the pancreatic deficiency, were of tremendous importance. Wine was then, as now, preferred as a source of food alcohol, because of its moderate concentration and the fact that wine drinkers seldom become intemperate. When the diabetic takes wines regularly in prescribed quantities with his meals, it serves as an excellent, predictable source of extra calories which do not require insulin for their assimilation.

Atwater and Benedict,[8] after exhaustive and conclusive research, demonstrated that alcohol had a coefficient of availability of 98 per cent; that the potential energy of alcohol was transformed completely into kinetic energy either in the form of heat or of muscular work; and that alcohol protected body fat and protein. Furthermore, they made the point that the alimentary digestion of alcohol did not interfere with the absorption of other foods, but in certain cases increased the efficiency of absorption.

Prior to the publication of Atwater and Benedict,[8] Zuntz and Magnus-Levy[205] had already found that alcohol did not lessen the utilization of food by the body, while Neubauer,[136] and Benedict and Török[18] had concluded, to their own satisfaction, that wine facilitated the oxidative processes in diabetics and enabled them to burn carbohydrates with lessened sugar excretion and with reduced acetonuria.

Beebe[17] and Mendel and Hildreth,[125] on investigating the facilitation of protein metabolism after ingestion of alcohol, found an increase in the output of uric acid, but no change in the nitrogen partition.

Gavrila and Sparchez,[77] Diner,[55] Kolta,[101] and Soula and Baisset[171] found significant decreases in the blood sugar levels of diabetics after ingestion of small amounts of alcohol. Burge[33] previously had noted this same decrease and attributed it to formation of a tissue enzyme, catalase.

Tennent [181] in a recent careful study finds the blood sugar level of the normal human being to be unaffected by ingestion of moderate amounts of alcohol.

Wiley [199] points out that the caloric value of alcohol at seven calories per gram is midway between that of protein and fat, while Porter [152, 153] points to the ready and complete availability of its value as a food. Barlow,[12] administering 7.5 per cent alcohol to young rats as the sole source of fluid, found that their growth rate was not impaired. Southgate [172] notes, as have many others, that the peak blood alcohol level when alcohol is taken with the meals is lower than that when taken without food.

The inclusion of wine in the diabetic diet has been recommended by Joslin [97] in this country and Conybeare [51] in England.

Dieticians have used the figures below when adding wine to the diet:

COMPOSITION AND FUEL VALUES OF WINES[27]

Wines:			Value of portion in grams.				
American Table Wines:	cc.	Portion	Alcohol	Carbohydrate	Protein	Fat	Calories
California red wines, Claret, Zinfandel, Chianti, Burgundy, etc.	100	Wine glass	10.0	0.5	0.2	0	75
California white wines, Chablis, Riesling, Rhine	100	Wine glass	10.5	0.5	0.2	0	75
California white wine, Sauterne	100	Wine glass	10.5	4.0	0.2	0	90
Champagne from California and New York State	100	Wine glass	11.0	3.0	0.2	0	90
American Dessert Wines:							
Catawba (white)	100	Wine glass	13.0	12.0	0.2	0	140
Muscatel	100	Wine glass	15.0	14.0	0.2	0	165
Port	100	Wine glass	15.0	14.0	0.3	0	165
Sherry	100	Wine glass	15.0	8.0	0.3	0	140

By prescribing wine to be taken with meals, several purposes are accomplished in the diabetic diet:

(a) It serves as an excellent and regular caloric source free from the need of insulin;

(b) The intake is regular, predictable and satisfying;

(c) It relieves the diabetic of social embarrassment;

(d) It makes an extremely regular diet more interesting;

(e) It does not interfere with the absorption of his regular diet, and

(f) It contributes to the patient's feeling of well being, and to his degree of cooperation.

USE OF WINE IN ACUTE INFECTIOUS DISEASES

The older practitioners used wines of many types freely in their treatment of infectious diseases. Anstie[6] wrote perhaps the best monograph on the subject crystallizing the attitude of his generation toward the therapeutic use of wine. He cautioned against the use of wine in more than moderate dosages but emphatically espoused the careful administration of wine in many diseases.

Primarily the benefits Anstie described were the toning of circulation, the reduction of fever through relaxation of skin arterioles, the increase in feeling of well being, a pleasant source of fluid to the exsanguinated, a stimulant in cardiac exhaustion, and a sedative for the delirious. He was particularly impressed by the effect of wine in intestinal diseases.

The clinician of today is largely unfamiliar with the medical practices of Anstie's time. In the light of present-day science the physician has been on the continual alert for the specifics, both chemical and biological, with which to combat the fevers, the malaise and the depressions that are found in every sick bed.

Prior to and during National Prohibition active and well financed campaigns were carried on against all uses of alcohol and as a result the physician prescribing wines or other beverages containing even small amounts of alcohol was put in an unfavorable light. Only recently has the pendulum begun to swing in the opposite direction.

None of the uses that Anstie so carefully discussed has been discarded.

The father of modern American medicine, Sir William Osler,[148] in speaking of wines states, "I should be sorry to give up its use in the severe form of enteric and pneumonic fevers." Recently in substantiation of this empiric statement it has been demonstrated by Himwich[86] that with the administration of alcohol in moderate concentrations the tissues remove less dextrose from the blood, since alcohol may take the place of foodstuffs in supplying energy to the body. Fantus[70] further amplifies this observation by noting that in fever alcohol is oxidized to a much greater extent than by the same person at normal body temperatures and concludes that its food value is of definite importance particularly in those cases in which digestion is impaired. This glycogen sparing effect should be a material aid to the overburdened liver of the debilitated fever patient.

Recently Soresi [170] has reported a long series of hospitalized patients that were given wine by proctoclysis with very gratifying results. In pneumonia it was given not only for its caloric value, but also for its cerebral effects. He made no claim for it as a specific but only as an adjunct to the usual treatment. He does make the note that recovery was more rapid and easy and that no deleterious effect was noted on the blood corpuscles nor on the urinary constituents.

Violle and Rosé,[187] in studying typhoid in Marseille in 1934, found that many inhabitants refused to add the prescribed amount of chlorine to their drinking water in the form of Javel solution because of the unpleasant chlorine taste. They found that 50 cc. of red wine added to a liter of the chlorinated water removed the excess chlorine and made the water highly palatable as well as acting as a mild disinfectant in itself.

It is interesting in conjunction with this to note that, according to Dougnac,[57] the incidence of typhoid in the wine drinking regions of France has generally been lower than in the regions where wine was less easily available. The well-known poor reputation of French drinking water has probably made the high per capita wine consumption in France a matter of intestinal self-defense.

Shorell,[168] in the treatment of sinus disease, advises the use of a light wine for its alkalinizing effect and quotes a sizable series of patients so treated that were benefited. He also points out the use of wine to stave off incipient delirium tremens in the acutely-ill alcoholic. This last observation is extremely frequent in the writings of the older clinicians.

USE OF WINE IN THE TREATMENT OF THE AGED AND THE CONVALESCENT

In the treatment of the aged and convalescent, wine has occupied a foremost position for generations. The values reported in earlier sections of this summary, particularly the stomachic, diuretic, diaphoretic, and vaso-dilating effects, agreeable taste, quickly-absorbed food value, and the comfort-giving and relaxing properties of wine, have made many physicians consider it absolutely necessary for the adequate care of the aged.

The older person with normally advanced arteriosclerosis is frequently querulous, forgetful, dyspeptic, dehydrated, and subject to many vagaries of digestion. To this group the effects derived from small amounts of wine are of great benefit. Galen [20] described wine as the nurse of old age.

The gentle sedation noted by Bishop,[22] Cornwall,[53] Horder,[87] Wood [202] and many of the older clinicians serves to dispel the fears and worries coincident with old age without acting as a cortical stimulant. Frequently the use of judicious amounts of dessert wine at bedtime (Horder [87]) will negate the need for barbiturate administration and cause a night of normal sleep to ensue.

Jacobi [93] and Thewlis [182] find the appetite of the aged increased by the administration of wine prior to mealtime. The generally lax and achlorhydric stomach of older people often requires the mild secretory stimulation that the physiologists, quoted in a previous section, have found following the ingestion of wine.

The gentle vasodilation following the taking of wine (Fantus [70]), according to Osborne,[146] aids the slowing cerebral circulation and promotes more normal cerebral cellular metabolism with resultant clarification of thought processes.

The increased intake of fluid with the ingestion of wine is quite desirable in the aged group, in whom intake of adequate fluid is generally recognized to be a difficult problem.

The iron content of natural wines from figures given by Bowes [25] would aid materially to combat the hypochromic anemia commonly found in this age group.

The toning of the colon and the facilitation of gastro-colic reflexes, as noted by Adler, Beazell, Atkinson and Ivy [2] stimulates the important evacuatory functions.

Leary [107] has been one of the foremost in stressing the role of alcohol in keeping body cholesterol in solution with a resultant decrease in the deposition of cholesterol in the intima of the blood vessels. In the aged, loss of arterial tone is primarily due to calcium deposition in these atheromatous plaques and the process, though it will not be reversed by the ingestion of wine, should be slowed.

The convalescent, regardless of his years, has many of the needs of the aged. He has an especial need for the increased digestion, lessening of worry, and promotion of relaxation obtained by the addition of wine to his diet.

WINE AS A VEHICLE FOR MEDICATION

The use of wine as a liquid vehicle for medicaments, after diminishing somewhat between 1918 and 1933, has increased substantially in more recent years.

Medical chemists find several peculiar advantages in wine over other alcoholic bases. The range of concentration of the alcohol in wine, from 7 to 21 per cent, is sufficient to keep in solution a number of relatively insoluble substances.

The mildly acid reaction, ranging from pH 3.5 to 4.2 for dessert wines and pH 2.9 to 3.8 for table wines [5] is of particular value in formulating medicines because so many of the commonly used therapeutic drugs are more soluble in a slightly acid solution. This degree of acidity is buffered strongly in the table wines and only a little less so in the dessert wines.

The buffering action is due to the presence of natural salts of potassium and sodium in the form of tartrates and phosphates. It is undoubtedly this buffering action that has been the basis for the successful white table wine extracts of belladonna root used with success in Parkinsonism. Fabing and Zeligs,[67] Neal and Dillenberg [135] and others have been unable to prepare a satisfactory decoction when other extractives were used.

The content of aromatic organic esters provides a pleasant and inexpensive flavoring which obviates the need for costly foreign or synthetic extracts.

Standards for Vinum Xericum, Vinum Portense, Vinum Alba, and Vinum Rubrum were prescribed in the U. S. Pharmacopoeia in all of its editions prior to 1918, at which time they were dropped coincidentally with National Prohibition. A long series of Vinum Medicata appears in dispensatories and formularies of virtually all other countries.

While it is well known that wine is universally used as a base for pharmaceutical preparations, the exact extent of its use is not measurable because the manufacturers do not disclose their trade secrets. Druggists' catalogues are replete with such preparations of all the major pharmaceutical houses. Improvement in wine production techniques has made it possible in recent years for the chemist to be more certain of the uniformity of his wine supplies, which varied appreciably in former years.

The wine type most frequently used in medical preparations is Sherry, with Port and a long list of other types occupying less important positions.

CONTRAINDICATIONS TO THE USE OF WINE

Although in past generations wine has been at various times used as a panacea for nearly all ills, the modern physician has, of course, no such misconception of its powers. Nevertheless, there are certain limitations which should be carefully observed in the use of wine and which warrant inclusion in this summary.

In general, it may be said that wine should not be used:

(a) In cases of acute inflammation;

(b) In cases of acute infection (pulmonary or generalized sepsis);

(c) In cases of acute nephritis or acute pancreatitis;

(d) In cases of shock, unless administered by one thoroughly trained in medicine;

(e) At times shortly prior to performance requiring accurate muscular coordination, or

(f) To such extent, or in such quantities, as to reduce the intake of basic dietary elements in their necessary proportions.

Like other foods, wine should not be used to excess.

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